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| 10/045,790 | 01/14/2002 | Richard A. Rosenbloom | QUIG-1006CIP | 3053 |

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| EXAMINER | |
|---|---|
| JIANG, SHAOJIA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/045,790 | ROSENBLOOM, RICHARD A. | |
| | Examiner | Art Unit | |
| | Shaojia A. Jiang | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 January 2005 and 29 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,9-20 and 38-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-20 and 38-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/29/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 24, 2005 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed March 24, 2005, and amendment and response to the Final Office Action (mailed October 20, 2004), filed January 24, 2005 and March 29, 2005 wherein claims 1-7, 9-20 and 38-42 have been amended; claim 42 is cancelled. Claims 8 and 21-37 are cancelled previously.

Currently, claims 1-7, 9-20, and 38-41 are pending in this application.

Claims 1-7, 9-20, and 38-41 as amended now are examined on the merits herein.

Applicant's declaration of Gerald H. Sokol, M.D. (not inventor), submitted March 29, 2005 under 37 CFR 1.132, is acknowledged and will be further discussed below.

Applicant's amendment filed on January 24, 2005 with respect to the rejection of claim 4 made under 35 U.S.C. 112 second paragraph for insufficient antecedent basis

of record stated in the Office Action dated October 20, 2004 have been fully considered and found persuasive to remove the rejection since the indefinite recitation has been deleted from the claim. Therefore, the said rejection is withdrawn as to claim 4.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the same reason of record in the previous Office Action October 20, 2004.

Note that claim 1 recites "one or more compounds selected from the group **consisting of**...." And "one or more antioxidants selected from the group **consisting of**...." (emphasis added). The transitional phrases "consisting of" employed in the claim is closed-ended and does exclude additional, unrecited elements or method steps. See also MPEP 2111.03. However, claim 5-6 employ "comprising vitamin D3" and the antioxidant "comprises" as transitional phrases. Hence, claims 5-6 are broader than claim 1 in regard to specific antioxidants by reciting "comprising". Thus, claims 5-6 encompass additional, unrecited elements besides those compounds selected from the group **consisting of** the Markush groups in claim 1. There is insufficient antecedent basis for these limitations.

### *Response to Argument*

Applicant's arguments filed January 24, 2005 with respect to this rejection made under 35 U.S.C. 112, second paragraph, for indefinite recitation, have been fully considered but are not deemed persuasive as further discussed below.

Applicant argues that claim 1 recites "comprising". Nevertheless, those active compounds and antioxidants are limited to the those in two Markush groups, even though the method comprising and the composition comprising recited in claim 1. Thus, the composition may comprise additional, unrecited elements or ingredients, other than vitamin D3 or antioxidants. Therefore, the rejection is adhered to claims 5-6.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-9, and 12- 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40

of copending Application No. 10/288,761 for same reasons of record stated in the Office Action dated October 20, 2004.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to the same method of the treatment comprising the same active agents as the claims of the instant application. Thus, these methods between in the copending application and in the instant application are seen to substantially overlap.

Thus, the instant claims 1, 4-9, and 12- 20 are seen to be obvious over the claims 1-40 of copending Application No. 10/288,761.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 4-9, and 12- 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 10/279,315 for same reasons of record stated in the Office Action dated October 20, 2004.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a method for the reduction or treatment of reactive and inflammatory dermatoses comprising the same active agents as the claims of the instant application. One of ordinary skill in the art would recognize that radiation injury in a patient would be reactive and inflammatory

dermatoses. Thus, these methods between in the copending application and in the instant application are seen to substantially overlap.

Thus, the instant claims 1, 4-9, and 12- 20 are seen to be obvious over the claims 1-25 of copending Application No. 10/279,315.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant requests deferral of these provisional obviousness-type double patenting rejections until such time as notice of allowance in said co-pending applications are received is noted. Nonetheless, for the reasons of record, said rejections are maintained at this point.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7, 9-20, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over KITA, K (WO 9718817, equivalent to 6,162,801), and Bissett (US 6,051,602, PTO-892), and Darr et al. (of record) in view of Shimoi et al. (of record) and Kim et al. (5,776,460, of record).

Kita discloses that vitamin D including vitamin D3 (cholecalciferol), is useful in a dermatological composition for the protection and treatment of the skin and scalp from harmful UV radiation. See 6,162,801, abstract, col.1 lines 22-24 and 51-67, col.4 lines 13-16, and col.8 lines 51 to col. 9.

Bissett (US 6,051,602) discloses that the instant one or more flavonoids (also known as polyphenols and are known to obtained from green teas extracts, including catechin, epicatechin, and rutin compounds) are useful in a method of reduction or treatment skin conditions in human resulted from environmental damage or extrinsic factors such as UV radiation, pollution, wind, heat or IR, low humidity, harsh surfactants, by topically applying a composition comprising one or more flavonoids, a pharmaceutically acceptable carrier broadly (e.g., PPG), and other active agents such as anti-inflammatory agents and anti-oxidants such as vitamin A (retinol or retinyl derivatives) and C (asorbic acid), with conventional skin care product additives such as kernel oil, panthenol, to human skin. See in Bissett, the abstract, col.1, col.2 lines 14-48, col. 3 lines 13-36 and 53-55, col.4 lines 13-16, col. 4 lines 65 to col. 5 line 49, col.6 lines 1-55, col.7 lines 1-10, Example 1 and 3 at col.9-10, and claims 1-11. Bissett discloses the effective amounts of one or more flavonoid compounds, about 0.01-20%, more preferably, about 0.1-10%, and most preferably about 0.5-5%, within the instant claim (see col. 5 lines 60-64).

Darr et al. discloses that vitamin C such as asorbic acid or vitamin E is useful in a composition to be administered orally or topically in the treatment of the protection of UV radiation-induced damage. See Summary and page 247.

The prior art does not expressly disclose the employment of the combination of vitamin D3 and ascorbyl palmitate and flavonoid / flavonoid derivatives, and ginseng in a composition to be administered in a method for the treatment or reduction of radiation injury. The prior art does not expressly disclose that the particular radiation is proton, fluoroscopic, alpha, beta, or gamma radiation.

Shimoi et al. discloses that flavonoid / flavonoid derivatives from plant or tea are antioxidants and have radioprotective effects. See abstract.

Kim et al. discloses that ginseng is known to be useful in the protection of radiation injury. See col.1 lines 21-27.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the combination of vitamin D3 and ascorbyl palmitate and flavonoid / flavonoid derivatives, and ginseng in a composition to be administered in a method for the treatment or reduction of radiation injury.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of vitamin D3 and ascorbyl palmitate in a composition to be administered in a method for the treatment or reduction of radiation injury since vitamin D such as vitamin D3 is known to be useful for the protection and treatment of the skin and scalp from harmful UV radiation. Antioxidants such as vitamin C (asorbic acid) is known to be useful in the treatment and the protection of UV radiation-induced damage. Moreover, ascorbyl palmitate is a known vitamin C (an ester of asorbic acid). Therefore, one of ordinary skill in the art would have reasonably expected that combining vitamin D3 and ascorbyl palmitate known useful for the same

purpose, i.e., treating radiation damage, in a composition to be would improve the therapeutic effect in treating radiation injury.

Further, both flavonoid / flavonoid derivatives and ginseng are known antioxidants and also known to be useful in the protection of radiation injury. Therefore, one of ordinary skill in the art would have reasonably expected that further adding both flavonoid / flavonoid derivatives and ginseng to the composition herein known useful for the same purpose, in a composition to be administered would provide additive effects for the therapeutic treatment in radiation injury.

Furthermore, one of ordinary skill in the art would have reasonably expected that the combination herein would have same or substantially same beneficial therapeutic effects in proton, fluoroscopic, alpha, beta, or gamma radiation, as in UV radiation-induced damage.

Since all active composition components herein are known to useful to treat radiation injury, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claims 5-6 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over KITA, K (WO 9718817, equivalent to 6,162,801), and Bissett (US 6,051,602, PTO-892), and Darr et al. (of record) in view of Shimoi et al. (of record) and Kim et al.

(5,776,460, of record), further in view of Ishida et al. (US 5141741, of record) or Nguyen et al. (US 5650137, of record).

The same disclosures of KITA, K, and Bissett et al. and Darr et al. in view of Shimoi et al. and Kim et al. have been discussed in the 103(a) rejection set forth above.

The prior art does not expressly disclose the employment of the particular antioxidant, alpha.-lipoic acid or chlorophyllin or superoxide dismutase in a composition to be administered in a method for the treatment or reduction of radiation injury.

Ishida et al. discloses that alpha.-lipoic acid and vitamin A, B, C, D, E, F, K, P, U are known to be useful in the protection of UV radiation or anti-sunburn in human skin. See abstract, col.5 lines 65-68.

Nguyen et al. discloses that superoxide dismutase or the porphyrins such as chlorophyllin, alone or in combination are antioxidants and have protective effects to human skin including against UV radiation. See abstract, col.1, col.2 lines 20-31, col.3 lines 40-66, claims 1-11.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular antioxidant, alpha.-lipoic acid or chlorophyllin or superoxide dismutase in a composition to be administered in a method for the treatment or reduction of radiation injury.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular antioxidant, alpha.-lipoic acid or chlorophyllin or superoxide dismutase in a composition to be administered in a method for the treatment or reduction of radiation injury, since alpha.-lipoic acid or chlorophyllin

or superoxide dismutase, alone or their combination is well known to be useful for the protection and treatment of the skin and scalp from harmful UV radiation, as those known antioxidants taught by the cited prior art.

Therefore, one of ordinary skill in the art would have reasonably expected that alpha.-lipoic acid or chlorophyllin or superoxide dismutase, alone or their combination would have the same usefulness and provide additive effects for the therapeutic treatment in radiation injury. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

***Response to Argument***

Applicant's arguments filed March 29, 2005 and January 24, 2005 and the declaration of Gerald H. Sokol, M.D. (not inventor), submitted March 29, 2005 under 37 CFR 1.132 with respect to the rejections made under 35 U.S.C. 103(a) of record in the previous Office Action October 20, 2004 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

The declaration of Gerald H. Sokol regarding the survival testing on mice under the radioprotection/treatment of radiation lethality induced by four MEV photons of ionizing radiation in mice, is insufficient to overcome the rejections made under 35 U.S.C. 103(a) for the following reasons.

First, Applicant avers unexpected benefits residing in the claimed subject matter, yet fail to set forth evidence substantiating this belief. Evidence as to unexpected benefits must be" clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and

be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA, 1972). In this case, a single specific composition consisting of water, Alpha Lipoic Acid, Baking Soda, Vitamin D3, Sodium Copper Chlorophyllin in specific amounts (see the formulation at page 3 of the declaration) was tested. Thus, the evidence in the examples herein is not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of the ingredients in the claimed composition. See MPEP § 716.02(d).

Second, it is noted that the declaration provides no side-by-side comparison with the closest prior art in support of nonobviousness for the instant claimed invention over the prior art, e.g., comparing the instant combination with the prior art compositions, and comparing the effects of the combination claimed herein in proton, fluoroscopic, alpha, beta, or gamma radiation, and in UV radiation-induced damage.

Thus, there is no clear and convincing evidence in the declaration for supporting the nonobviousness or unexpected results for the method herein over the prior art. Therefore, the declaration is insufficient to rebut the prima facie case of obviousness herein.

Again, Applicant asserts that Kita dose not teach a vitamin D to be administered orally in the claimed method herein in treating radiation injury in a human. Contrary to Applicant's assertion, Kita teaches that "Therapeutic vitamin D is administered orally or by injection, and is applied to the skin as an active vitamin D ointment in the case of skin conditions" (see col.1 lines 42-44 in particular). Kita further teaches that "It is known that the molecular structure of vitamin D is altered in the liver and kidneys, converting it

into biologically active vitamin D" (see col.1 lines 44-46 in particular), and "It is now known that there are active vitamin D receptors in the cells, and the inhibition of cell activity is being studied since active vitamin D inhibits the production of a variety of cytokines" (see col.1 lines 63-67). Moreover, Kita teaches that "In general, the ultraviolet (UV) light absorption spectra of vitamin D and active vitamin D have absorption maxima 265 nm, with the molar absorption coefficients of about 18,000". See col.1 lines 25-28. Hence, one of skill in the art would recognize that the molar absorption coefficients of UV radiation for vitamin D are very high. Therefore, based on the teachings of Kita, one of ordinary skill in the art would have found it obvious to administer a vitamin D orally in treating radiation injury in a human. Additionally, oral administrations of vitamin D or D3.

Furthermore, as indicated in the previous Office Action, since all active composition components herein are known to useful to treat radiation injury, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

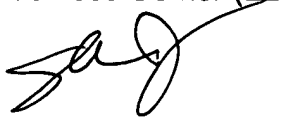
For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejections are adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Art Unit 1617
June 3, 2005